

PX3813US
Serial No. 10/018,878

In the Claims

Please amend the claims as shown below.

Please cancel Claim 49

1. (Previously presented) A DNA construct comprising a transcriptional unit which comprises a ribonucleotide reductase gene wherein the ribonucleotide reductase gene comprises a T4 *nrdA* gene modified to comprise SEQ ID No. 9.

2. (Previously presented) A DNA construct as claimed in claim 1 comprising a transcriptional unit further comprising a T4 *nrdB* gene and a thioredoxin gene wherein the thioredoxin gene is a T4 *nrdC* gene.

3. - 4. (Canceled)

5. (Previously presented) A DNA construct according to claim 2 wherein the construct is a vector.

6. (Previously presented) A DNA construct according to claim 5 wherein the vector is a virus, transposon, minichromosome or phage.

7. (Previously presented) A DNA construct according to claim 6 wherein the vector is a plasmid, and wherein the modified T4 *nrdA* gene the T4 *nrdB* gene, and the T4 *nrdC* gene are arranged in an operon.

8. (Previously presented) A DNA construct according to claim 7 wherein the transcriptional unit comprises the modified T4 *nrdA* gene and the *nrdB* gene, and wherein the modified T4 *nrdA* and T4 *nrdB* genes are located downstream of the T4 *nrdC* gene.

9. (Canceled)

PX3813US
Serial No. 10/018,878

10. (Previously presented) A DNA construct according to claim 8 wherein the T4 *nrdC* gene is upstream of the modified T4 *nrdA* gene and the modified T4 *nrdA* gene is upstream of the T4 *nrdB* gene.

11. (Original) A DNA construct according to claim 6, further comprising a regulatory element.

12. (Original) A DNA construct according to claim 11, wherein the regulatory element is selected from the group consisting of a promoter, an operator, a termination sequence, an initiation sequence and a ribosome binding site.

13. (Original) A DNA construct according to claim 12 wherein the promoter is the lambda P_L promoter or a derivative therefrom.

14. (Previously presented) A DNA construct according to claim 12 wherein the termination sequence is a heterologous terminator sequence.

15. (Previously presented) A DNA construct according to claim 1 wherein the modified T4 *nrdA* gene is modified such that the ribonucleotide reductase encoded by the unit is less sensitive to allosteric inhibition than the wild type equivalent of said ribonucleotide reductase encoded by the unit comprising an unmodified *nrdA* gene.

16. - 20. (Canceled)

21. A DNA construct according to claim 4 wherein the construct further comprises a T4 *td* (thylidymate synthase) gene.

22. - 23. (Canceled)

PX3813US
Serial No. 10/018,878

24. (Previously presented) A DNA construct according to claim 21 wherein the *td* gene is located in the same operon as the *nrdA*, *nrdB* and *nrdC* genes.

25. (Previously presented) A DNA construct according to claim 24 wherein *td* gene is located downstream from the modified *nrdA*, *nrdB* and *nrdC* genes.

26. - 28. (Canceled)

29. (Previously presented) A DNA construct according to claim 2 further comprising an E.coli uridine kinase gene or an E. coli dCTP deaminase gene.

30. (Previously presented) A DNA construct according to claim 29, wherein the DNA construct comprises both an E.coli uridine kinase gene and an E.coli dCTP deaminase gene.

31. (Previously presented) A DNA construct according to claim 1-30 wherein the E.coli uridine kinase gene is a *udk* gene. ~~3, 4, 9, 16-20, 22, 23, 26-28, 30, 39, 42 and 47~~

32. (Previously presented) A DNA construct according to claim 30 wherein the E.coli dCTP deaminase gene is a *dcd* gene

33. (Previously presented) A modified E.coli host cell comprising a DNA construct according to any one of claims 1, 2, 5-8, 10-15, 21, 24, 25, or 29-32.

34. (Previously presented) A modified E.coli host cell according to claim 33 wherein the host cell displays repressed or no uracil DNA glycosylase activity.

PX3813US

Serial No. 10/018,878

35. (Previously presented) A modified *E. coli* host cell according to claim 34 wherein one or more host cell DNA polynucleotides encoding for uracil DNA glycosylase activity have been modified so as to encode expression products displaying repressed, low levels of, or no uracil DNA glycosylase activity.

36. (Previously presented) A modified *E. coli* host cell according to claim 35 wherein the modified host cell DNA ~~polynucleotides~~ polynucleotide comprises an *ung* gene.

37. (Previously presented) A modified *E. coli* host cell according to claim 34 wherein one or more host cell DNA polynucleotides encoding for uracil DNA glycosylase activity have been removed.

38. – 39. (Canceled)

40. (Previously presented) A modified *E. coli* host cell comprising a DNA construct, which construct comprises a transcription DNA unit, which unit comprises a ~~modified T4 *nrdA* gene~~ modified T4 *nrdA* gene comprising SEQ ID No 9, and a T4 *nrdB* gene ~~encoding a ribonucleotide reductase~~ and a T4 *nrdC* gene, wherein the modified T4 *nrdA* gene encodes a said-ribonucleotide reductase ~~displays less sensitivity which is less sensitive to allosteric inhibition~~ than the wild-type equivalent of the reductase, and wherein said host cell further comprises one or more of the following features:

- (a) a transcription unit located on said DNA construct, comprising a thymidylate synthase gene heterologous to the thymidylate synthase gene of the host cell;
- (b) a transcription unit located on said DNA construct, comprising an *E. coli* uridine kinase gene;
- (c) a transcription unit located on said DNA construct, comprising an *E. coli* dCTP deaminase gene; and

PX3813US
Serial No. 10/018,878

(d) repressed or absent uracil DNA glycosylase activity.

41. (Previously presented) A modified E.coli host cell according to claim 40, wherein the ribonucleotide reductase gene is modified at a dTTP binding site.

42. (Canceled)

43. (Previously presented) A modified E.coli host cell according to claim 40, wherein the DNA construct comprises both the uridine kinase gene and the dCTP deaminase gene.

44. (Previously presented) A modified E.coli host cell according to claim 40, wherein the cell comprises each one of the features of (a) to (d).

45. (Previously presented) A process for the production of pyrimidine deoxyribonucleosides comprising culturing a host cell according to claim 33.

46. (Original) A process according to claim 45 wherein the deoxyribonucleoside is thymidine.

47. (Canceled)

48. (Previously presented) A culture medium comprising a host cell according claim 33.

49 (Canceled)